Psoriasis

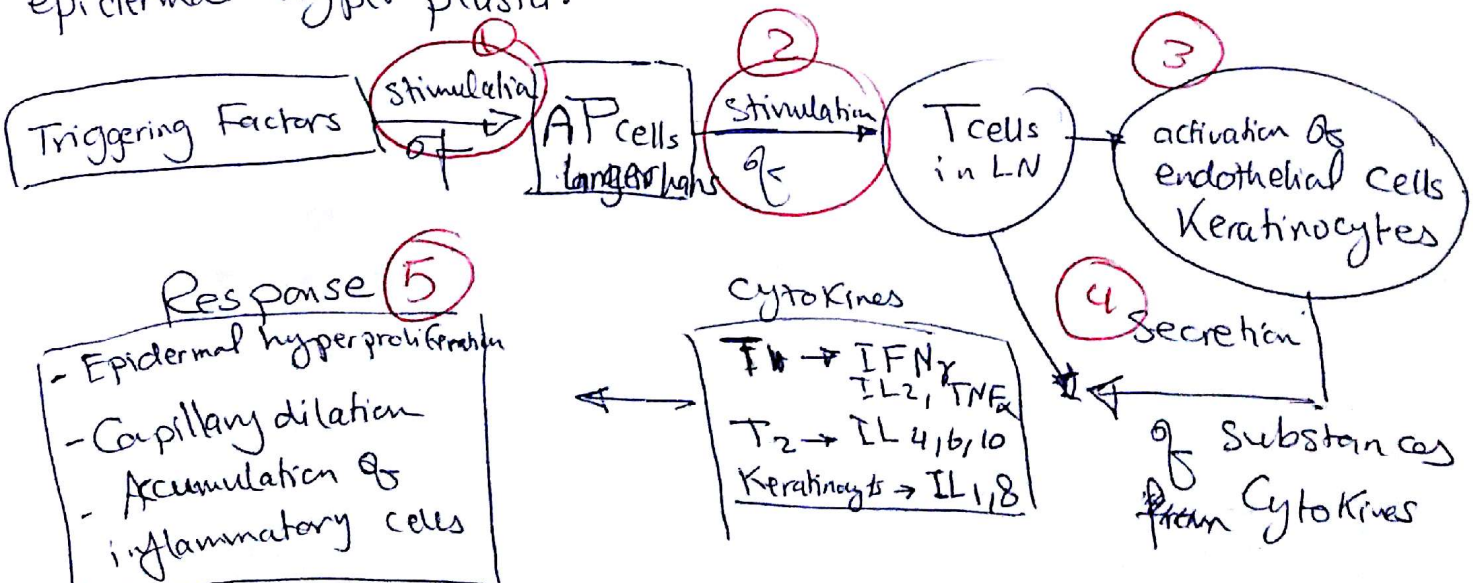
- Common chronic skin disease with remissions and relapses affect 1-2% of population with no age relationship.

Provocative Factors:

1. Genetic :- 30% of patient have +ve Family history
   - ↑ incidence of HLA-B13, HLA-Cw6
   - if both parents affected the chance of the child is 50%
   - if only one parent affected " " " " 16%
2. Trauma : may induce psoriasis (Koebner phenomenon)
3. Infection : Strept. preceed guttate Psoriasis via superantigen activation of T-cells
4. Weather :- Winter worse the condition but summer improve it
5. Endocrine : Psoriasis ↑ at puberty, menopause and ↓ in pregnancy
   Hypocalcemia ↑ pustular psoriasis.
6. Drugs : Antimalarial, β-blockers, NSAID, Lithium, Interferon
7. Stress : aggravate psoriasis in 40%
8. Others : obesity, smoking, Alcohol → ↑ psoriasis.

Pathogenesis of Psoriasis :-

Psoriasis is a T-cell mediated inflammatory process that leads to epidermal hyperplasia.



pathogenesis of Psoriasis.

triggering Factors → activation of APC → migration to LN
(Stress - Genetic - Trauma - infection)
in Langerhans cell

LN → activation of Tcell → differentiation < T_1 / T_2

activation of Keratinocytes + Endothelial cells → cytokines

Cytokines → action :-

Th_1 → TNF-α ↓ by ↓ apoptosis
Keratinocyte → ↑ proliferation → plaque
Endothelial cells → extravasation
& T-cells → Vascular endothelial growth Factor (VEGF) → Angiogenesis → Erythema

Th_{17} → IL 17 → Keratinocytes (increased expression of Certain Chemokines that result in Th 17 recruitment (+ve feed back) and neutrophils chemotaxis (histopathology → Munro's and Kogoj microabscess + ↑ Human β-defensin (1) HBD1 → pro-inflammatory activity + Antimicrobial

Th_{22} → IL 22 → Keratinocyte proliferation. (plaques).

Histopathology of Psoriasis

[1] Parakeratosis: Retention of nuclei in st. corneum ~~with~~ munro microabscess (due to migration of neutrophiles transepidermally from dilated capillaries in dermal papillae)

[2] Absence of granular cell layer

[3] Acanthosis: Thickening of epiderms + Regular elongation of Rete ridges with thicking of lower portion (Clubbing)

[4] Elongation and edema of dermal papillae ⟨ club shape + dilated capillaries in upper portion

[5] Relative thinning of supra papillary portion of st. malpighii NB number (4) + (5) = Auspitz sign.

[6] Spongiform pustule of Kogoj (diagnostic) very small spongiform pustules in st. malpighii.

[7] Perivascular mononuclear cells infiltrate in upper dermis.

Clinical picture of Psoriasis

SDR PS LS

- Sharply Demarcated Red papules or plaques covered with Silvery laminated scales (Psoriasis vulgaris)

Distribution: usually symmetrical but can occur in any place mainly (extensors, Sacral region, Scalp, nail)

Grattage test: pin point Hge

Scraping of psoriatic lesion by edge of glass slide result in Removing scales (layer by layer) until a thin membrane Left → if this membrane removed → Pin point Haemorrhage appears. (Auspitz sign).

Clinical Forms

According to Morphology	According to site	Pustular Form
2GP AFDL [illegible]	F 2SAPNE [illegible]	localized Acute Generalized

[1] Morphology

Guttate
minimal scaling.
size of lesions like drops of water (may follow acute strept. infection)

Geographic
Multiple annular lesions connected together in large areas as the back.

Annular ○
Ring shaped lesion produced by involution of the center.

Plaque: (classical) = (Psoriasis vulgaris) = the most common type 85–90 %

Follicular: prominent follicular lesion in female ~~thigh~~ or child back.

Discoid: Coin shaped Lesion.

Linear and Zonal

[2] Site

- **Flexural** | in flexures areas. there's no scales in these areas because of continuous friction and moist itching is more common (shiny) pink to red
- **Scalp** | Discoid lesion or band-like plaque along the ant. hair line. Telogen effluvium is common.
  D.D seborrheic dermatitis

NB **Pityriasis amiantacea**: a case of soft patches with firmly adherent asbestos-like scaling it's non specific reaction occur in psoriasis (commonly) and others (seborrheic D)

- **Seborrheic Psoriasis** (seboPsoriasis)
  pt with psoriasis + seborrhic dermatitis (both symptoms)

- **Arthritis** (Psoriatic arthropathy):
  - in 5-30% of pt with Cutaneous Psoriasis. Rheumatoid Factor -ve
  - ↑circulating TNF
  - Nail affection is common (80-90%)
  - it's presented by * dactylitis (swelling of Fingers)
    * enthesitis (inflammation of insertion of tendons and Ligaments)

  X-ray shows Pencil in Cup deformity (distal head of bone is sharpe like a point) + Fusiform tissue swelling (sausage digit) + Tuft resorption + eccentric erosions.

- **Palm and sole**: may presented by:
  1. Typical silvery scaly patches
  2. Thick fissured plaques
  3. palmo-plantar pustulosis
  4. Mixed forms.
  5. Rupioid on sole (cone shaped plaques + thick dark, lamellated, adherent crusts)

- **Nail** 25-80% of Pt.

  affect nail matrix, Nail bed

  1. Nail matrix → Retention of nuclei in some areas of nail Keratin lead to weakness shedding of these areas → pitting + grooves + ridges
  2. Nail bed → Subungual hyperKeratosis + onycholysis splinter haemorrhage + oil drops (salmon patches) discoloration.

℞ 5-Fluorouracil Topical OR Triamcinolone intra Lesional by dermojet

④ **Erythrodermic**:

- Characterized by Generalized Erythema and scaling (90% of the body surface) Commonly precipitated by infection, hypocalcemia, antimalarial, steroid withdrowal
- Clue of Diagnosis (Past history of Psoriasis + Nail changes + Facial sparing) lab ↑leucocytosis + ↑ ESR

other sites of psoriasis

[1] Mucosal (oral, ocular)

oral: annular erythematous lesion with hydrated white scale

ocular: can affect any part of the eye.

[2] Penil (Typical lesion) psoriatic plaques + white scale

No scales on glans of uncircumcised penis.

[3] Pustular Psoriasis

It's characterized clinically by sterile pustules and pathologically by increased neutrophil accumulation in

① Stratum Corneum → Munro micro abscess.

② stratum spinosum (malpigii) → Kogoj micro abscess.

Pustular psoriasis

Generalized

large area or whole body

Sub-acute, acute, life threating

① Acute (von zumbusch)

② Pregnancy (Impetigo herpetiformis)

③ localized (except hand, Foot)

④ Exanthematic

⑤ Infantil

Localized

limited (hand, Feet)

Chronic

① Palmoplantar Pustulosis (PPP)

② Acrodermatitis Continua of hallopeau.

Generalized pustular psoriasis (GPP)

General triggering Factors :-

Pregnancy - Rapid steroid withdrawal - Hypocalcemia
infection - irritation by topical therapy (coal tar)

Types ① Acute GPP von zumbusch

C/P Burning sensation → Pain in skin, Fever, malaise develops into sheets of erythema and studded with pustules. the pustules are sterile. perefers flexular areas. the pustules resolve with scaling (dried)
Nail → thick - onycholysis by subungual lakes of pus
Tongue → may be involved (geographic tongue)

Complications → ① Progression to generalized erythroderma.
② Hypoalbuminaemia ③ Hypocalcemia ④ Oligaemia
⑤ Acute Renal tubular necrosis (fatal)
⑥ DVT and Pulmonary embolism (fatal) ⑦ infection (Staph)
⑧ Polyarthritis. ⑨ Hair loss (TE) ⑩ Liver damage
⑪ Amyloidosis (Rare).

Lab ↑ Leukocytosis ↑ ESR Hypo < Albuminaemia, Calcemia, Zinc

Treatment of GPP

- Topical Treatment is not effective
- Removal of triggering factors.
- Hospitalization, bed rest, I.Venous fluid.
- Systemic treatment
  - Acitretin is the drug of choice
  - Methotrexate, Cyclosporine, PUVA, Biologics

in pregnancy prednisolone is the drug of Choice and Methotrexate + PUVA after delivery.

② GPP of pregnancy

Rare, occur in last trimester, associated with hypocalcemia and ↓ vit D / it's Recurrent in subsequent pregnancies and using of oral contraceptive pils.

CIP is the same of Acute GPP Complication is the same + placental insufficiency ⟶ Still birth, neonatal death fetal abnormalities. ℞ prednisolone NO PUVA or Retinoid

③ Circinate (annular) GPP

Annular lesions enlarged by centrifugal expansion with central healing. pustules are at the periphery. it will dry and leave trailing fringe of scales

④ Localized form of GPP

pustules appears within or at the edge of pre-existing psoriatic plaques. D.D pulmoplantar pustulosis (PPP)

⑤ Exanthematic GPP

Acute self limited eruption of small pustules following infection or drug. No systemic symptoms.

⑥ Infantil GPP

Rare at child hood - More in male - benign
No systemic symptoms - Any form can occur but Annular form is common.

Localized pustular Psoriasis

1 Palmoplantar Psoriasis (PPP)

- Bilateral, Symmetrical Sterile pustules of palmoplantar surface with yellow brown macules (dried pustules)
- Triggering factors: infection (Tonsillitis), Smoking, Lithium, Stress, TNF-α antagonist
- it's chronic course resistant to treatment
- Associated with SAPHO syndrome (Synovitis, Acne, pustulosis, Hyperostosis, Osteitis)

2 Acrodermatitis Continua :-

- Rare. pustules are found on the tip of finger or Toe then followed by scaling and crust formation.
- pustules may affect the nail bed (beneath the nail) Leading to nail dystrophy, Shedding.
- usually associated with oral Lesions (annulus migrans)

Treatment of Psoriasis

1) General measures

* Weight Reduction
* avoid emotional stress
* Avoid Trauma (physical, sun burn)
* Reassurance, counseling
* Rest
* Diet (↑ diet with oil fish)

2) Topical treatment:

(a) Topical Corticosteroids

- 1st line treatment as monotherapy or in combination.
- 1-2 times daily for short period only 2-4 weeks.
- Mechanism of action: Anti-inflammatory * Antiproliferative * immunosuppressive * Vasoconstrictive.
- S.E: skin atrophy - telangiectasia, striae, purpura
  Contact dermatitis - if used around eye → (Glucoma, Cataract)
- Contra-indications: ⊙infection (bact., viral, fungal) ⊙Allergy to CST
- Intralesional CST (Kenacort) for small localized lesion OR Nail Psoria
  Pregnancy Category C

(b) Topical vit. D_3 Analogues (Calcipotriol)

- oint, cream, lotion 50 mcg. the dose twice daily and not exceed 100 g/week. * improvement after 2 weeks and Complete healing within 8 week.
- Mechanism of action: it bind to vit. D receptors. lead to
  * ↓ Keratinocyte proliferation * Normal Keratinocyte differentiation
  * Immunomodulatory effect
- S.E - transient irritation. (avoid Face, Flexural area better add CST)
  - Dryness - erythema - Peeling, edema.
  NB Salicylic acid should not used at the same time Cause it inactivate Calcipotriol)
  systemic Reversable hypercalcemia + Parathyroid Hormon Suppression.

Contra indication of Calcipotriol:

→ Involvement requiring > 100 gm/ week , → Allerg →

→ Pregnancy , Lactation → Renal insufficiency

→ Abnormal bone marrow or Calcium metabolism.

② Topical Anthralin

Short contact therapy start by 1% concentration then increase by time. to decrease irritation.

Mechanism of action: → inhibit T cell activation

→ Normalize Keratinocyte differentiation.

→ Anti- hyperproliferative.

S.E staining - irritation

Contra-indications: - Pustular , Erythrodermic psoriasis.

- Avoid Face , Flexural areas cause high irritation

Ingram technique: Tar bath + UVL + Anthralin.

③ Topical Coal Tar: safe but messy.

mechanism: Anti- mitotic (supress DNA synthesis) Anti- inflammatory

Anti- pruritic.

S.E Folliculitis - Acne form eruption - irritation (Contact dermatitis)

Carcinogenic in animals

Contra-indication → Pregnancy, lactation, children (Mutagenic effect)

→ Pustular and Erythrodermic psoriasis.

Goeckerman technique:- Crude coal tar oil + UVB light.

④ Topical Retinoid (Tazarotene)

once daily at night - Not inactivated by UVA or UVB

Mechanism ① ↓ Keratinocyte hyperproliferation ② Normalize K differentiation

③ ↓ expression of inflammatory cytokines.

S.E - irritation - pruritis - teratogenicity - Photosensitivity

Contra indication Pregnancy

NB to reduce irritation we add corticosteroids.

(F) Topical Salicylic acid

mechanism: → Reduce Keratinocyte to Keratinocyte binding
→ Reduce PH of st. corneum → ↓ scaling + ↑ softening

S.E Systemic toxicity so avoid to use with oral Salicylates

NB if combined with CST it improve penetration → ↑ effecacy

(G) Topical Calcineurin inhibitors Tacrolimus - pimacrolimus

mechanism: inhibition of T-cell activation by inhibiting Calcineurin phosphatase

S-E - Burning - itching

Best Combination therapy

- Calcipotriol + CST
- Salicylic A + CST
- Tazarotene + CST
- Tacrolimus + Salicylic

Combination with phototherapy → Ingram / Goeckerman

(2) Systemic Treatment

indication: Chronic large plaque - Erythrodermic Ps - P. arthritis
nail Ps.

Most common drugs: Methotrexate - Retinoids (Acetritin)
Cyclosporine - Biologics.

	Methotrexate	Acitretin	Cyclosporine
Mechanism of Action	Folic acid analog - inhibition of DNA synthesis of proliferating cells. Proliferating cells are effected earlier than Bone Marrow, hair, GIT	Correction of Keratinocyte differentiation - ↓ neutrophil migration.	selective immunosuppressant → Inhibit T-cell activation → inhibit Keratinocyte proliferation
Dose	Triple dose therapy. 3 times weekly every 12 hours tab. 2.5mg. maximum dose 30 mg/week after improvement ↓ the dose to 2.5 mg/month better to add Folic acid → ↓ Nausea, ↓ Macrocytic anaemia.	• Single daily dose for 3-6 month (10-50 mg)	2.5-5 mg ~~twice~~ daily in (2) divided dose for less than 1 year Decrease the dose if: • S-creatinin > 30% of (normal) - ↑ BP
Side effects	Nausea, Malaise, Stomatitis, Liver → hepatotoxicity Bone → BM suppression Lung → pulmonary Fibrosis, toxicity, dyspnea Reproductive oligospermia, Abortion, teratogenic	teratogenic - Hyperlipidemia Cheilitis - xerosis Hepatotoxic	Nephrotoxic - Hypertension- Malignancy, hypertrichosis Gingival hyperplasia. electrolyte abnormalities.
Contra Indication	Pregnancy - Hepatitis - Liver cirrhosis TB - peptic ulcer - Anaemia ↓ Renal Function.	pregnancy, lactation, DM hyperlipidemia, Liver or renal impairment. - Alcohol	HTN, ↑ Renal impairment Malignancy. pregnancy (C)
Monitoring of:	Liver profile. CBC, Renal profile Chest X-ray. HIV testing	Lipid profile, CBC, Kidney	BP, Renal function urea, S-creat. Lipid ~~function~~ profile.

[3] Biologic immunotherapy

Biologics: are protein that bind to extra cellular substances (proteins, receptors, cytokines) to block the activation in one or more step of the pathway of T-cell immune response

(a) targeting the pathogenic T.cell (CD_2) [Alefacept]
bind to CD_2 surface lead to → Apoptosis via perforin/granzyme System → depletion of activated T. cells

(b) targeting T.cell activation:- [Efalizumab] CD_{11}
block both Tcell activation + trafficking into the skin
but don't deplete T.cells (withdrown from Market)

(c) Immune deviation:
Administration of Exogenous Cytokines (IL4, IL10, IL11) deviate the differentiation of Tcells → imbalance of T_1/T_2 balance.

(d) Inhibition of cytokines (Anti cytokines)

- Anti TNFα → Etanercept → Adalimumab (Humera) 40 mg
  → Infliximab
  Dose Initial dose (80) →
  Then Followed by (40) in day 8 then (40) every 2 weeks.
- Anti IL12, IL23 Ustekinumab (stelera)
  IL12 → development of Th_1 IL23 → development of Th_{17}

side effects:
[1] ↑risk of infection or Reactivate latent infection eg TB
[2] ↑ risk of Malignancy. [3] hyper sensitivity
[4] C.V.S, CNS complication
Baseline monitoring in follow up:-
CBC, Renal, Liver functions. HIV testing
Hepatitis B/C serologically.

[4] Photochemotherapy

Photo therapy → Rx with UVR + (chemo) Combination eg Psoralene

Photo sensitizer eg (Psoralene) Topical & Methoxalen Tab

290–320

UVB Broad band

311–313 UVB Narrow band

* Mechanism of action:
- Anti-proliferative for Keratinocyte by ~~Infi~~ ↓ DNA synthesis
- Immunomodulatory: depletion of APCs, shift cytokine profile
- indications → Moderate to severe ps which not respond to Topicals
  - → Liver damage (Contra-indicated to Methotrexate)
  - → ~~old~~ Widespread Ps including Pustular, Erythrodermic

Side effects: Acute → erythema, burn, tanning, ↑ risk of infection

Facial dermatitis — photosensitivity, Hypertrichosis, Itching

Chronic → Photoaging + ↑ Skin Cancer

S.E of Psoralin → N, V, hepatotoxicity.

[5] Photodynamic therapy (PDT)

Small plaques. Application of photo sensitizer 5 amino laevulinic acid + light Blue/red

S.E → pain.

[6] Laser therapy

- → pulsed dye laser 585 nm obliterate vascularity in Ps
- → Carbon dioxide 10600 nm
- → Excimer high dose 308 nm equal narrow band UVB 311–313

[7] SPA therapy

bathing in Red sea or Dead sea - Balneotherapy